REMARKS

Claim 3 has been canceled as it was mistakenly included among the pending claims. It originally depended from claim 2 which related to the reverse (non-elected) process. The dependency of claim 12 has been corrected as clearly in error. Entry of this formal amendment, though after final, is believed proper. Claims 1 and 4-12 remain pending.

The invention lies in the discovery that acylases in general, and peptide deformylases in particular, are effective in hydrolyzing formyl groups from α-aminonitriles with stereospecificity. This was unknown prior to the present invention. The document cited by the Office, Sonke, T., *et al., J. Mol. Catal. B: Enzyme.* (2004) 29:265-277 as evidence of such knowledge is published three years subsequent to the filing date of the present application, and is the work of the present inventors. It cannot properly be cited in support of a rejection based on obviousness (as opposed to inherent anticipation).

The rejection under 35 U.S.C. § 112, paragraph 2, has been obviated by the cancellation of claim 3.

Rejection Under 35 U.S.C. § 112, First Paragraph

All claims were rejected as assertedly failing to comply with the written description requirement based on the holdings in the *University of California v. Eli Lilly*, 119 F3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997); and *Fiers v. Revel*, 984 F2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993). It is noted that this rejection is not based on lack of enablement, nor is it based on asserted overbreadth. It is grounded in the proposition that the structural aspects of the acylases claimed must be described in detail in the specification in order to support the invention as claimed. The quotations set forth in the Office action from *Lilly* and *Fiers* are accurate, but fail to take account of

the nature of the present invention and the knowledge in the art concerning, in particular the peptide deformylases useful in the claimed method, and the ready availability of acylases in general.

First, the claims are not directed to new acylases *per se* or to genes encoding them, but rather to methods which employ these enzymes. Of course, one must have the enzymes available in order to perform the process, and a description of the process would not be complete without describing the use of the enzymes in it (as opposed to describing the enzymes themselves). There is no assertion that one could not obtain the appropriate acylases for use in the invention or would not recognize what they are. With respect to claim 4, this is particularly true of the peptide formylases. As noted in the specification, peptide deformylases as a family are very well known in the art. See page 3, line 16 through page 4, line 35. As noted on page 3, lines 4-18, these well known enzymes are even formally classified in the EC. The same is true of acylases in general, many acylases are available in the art, and the practitioner would have no problem identifying them as such.

The analogy drawn between the present case and *Lilly* and *Fiers* is inappropriate. The Office states that the written description requirement is not met because acylases are included with "widely differing structural, chemical and physical characteristics from many biological sources -- the genus is highly variable because a significant number of structural differences between genus members exist." All of this is true, but irrelevant to the facts in the present case. What is required in the present case is not a description of any structural characteristics of the acylases, but rather of their activity, which is inherent in the term "acylase" itself.

Both *Lilly* and *Fiers* involved claims that were directed to new and unknown nucleic acids. The invention lay in the discovery of the new and unknown nucleotide sequences themselves. For example, in the *Lilly* case, the specific reverse transcripts of the mammalian proinsulins claimed

were completely unknown. The invention lay in elucidating this structure. Similarly, in *Fiers*, the gene encoding β-interferon was unknown and the invention lay in sequencing the gene. In contrast, here, the invention is directed to a process which merely employs well known enzymes readily available in the art and recognized by any practitioner. There is virtually no analogy in the nature of the claims or the nature of the prior art between the present claims and the situation in either *Eli Lilly* or *Fiers*.

Applicants note that it is not only the Examiner who seems to have misconstrued the requirements set forth in the two cases cited. Fortunately, the Federal Circuit has clarified the nature of the requirement for structural features in the recent case of *Capon v. Eshhar v. Dudas (as intervener)*, 418 F3d 1349, 76 USPQ 1078 (Fed. Cir. 2005). The Court reversed the rejection of a claim to chimeric DNA encoding a signal sequence, a binding domain from a single-chain antibody, a transmembrane domain, and a cytoplasmic signal transducing domain. Presumably the protein encoded would be displayed on the surface of cells and permit activation of these cells with an appropriate ligand. The Board had decided based on "controlling precedent" (probably *Lilly*) that the specification required "the complete nucleotide sequence of at least one chimeric gene." The Court explicitly stated that this was not a *per se* rule. The components of the chimeric DNA were well known in the art, and the invention lay in their combination, not in the sequence of any individual portion. The Court remanded with instructions that the Board explore the support for each of the claims in view of the specific examples and general teachings in the specification and known science.

Thus, the very limited holdings in *Lilly* and *Fiers* are inapposite here. Even if the proteins themselves were being claimed, complete structural information would not be required. See

In re Wallach, 378 F3d 1330, 71 USPQ2d 1939 (Fed. Cir. 2004) where claims to a new protein were upheld based on the disclosure of only a short N-terminal sequence in combination with other properties, such as function and molecular weight. Even these requirements are not appropriate here, where acylases are a very well known and very well understood class of enzymes. For these reasons, the rejection for lack of written description may properly be withdrawn.

The Obviousness Rejection

Claims 1, 4-9 and 12 were rejected as obvious over Rajagopalan, *et al., Biochemistry* (1997) 36:13910-13918. It is noted with appreciation that claims 10 and 11 are not included in this rejection, and so these claims are in a position for allowance if the rejection for written description is overcome.

The primary reference teaches that *E. coli* peptide deformylases have exactly that activity (deformylation) with respect to peptides. There is no teaching in Rajagopalan that this enzyme would be effective on α-aminonitriles or, indeed, that it requires a particular configuration of the substrate nitriles.

This cannot be remedied by the cited 2004 paper authored by the inventors themselves. The Office is reminded that this is not a rejection based on inherent anticipation (*i.e.*, an explanation of what was actually disclosed in Rajagopalan) in which case the 2004 paper would at least be relevant. Since the rejection is based on obviousness, the later discovery by the present inventors that the peptide deformylases are active on α-aminonitriles is not appropriately cited.

The third and fourth documents cited are not germane to the obviousness of the invention; they merely demonstrate what applicants have already noted in their specification, that peptide deformylases are well known in the art. Accordingly, the rejection over the art may properly be withdrawn.

Conclusion

It is clear from the documents cited by the Office itself that acylases, and in particular peptide deformylases, are well known in the art with regard to activity and availability. As these well known compounds are those employed in the process of the present invention, failure to provide detailed structural characteristics of these enzymes in the specification does not constitute a failure to provide adequate written description. The holdings in *Lilly* and *Fiers* were made in connection with different types of claims in an entirely different nexus with the state of the art. They are not appropriate to judge written description herein. More germane is *Capon v. Eshhar v. Dudas* which holds that even where the subject of the claims is a DNA molecule itself, the specification need not contain a detailed structural description of the claimed DNA in terms of sequence where the components of the sequence are well known in the art.

The secondary reference showing that peptide deformylases are active on α-aminonitriles is the later-published work of the inventors themselves. It is not properly citable against the present claims. There is no suggestion in the primary reference that such activity would be found, or that such activity would be stereospecific.

Accordingly, applicants believe that claims 1 and 4-12 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 246152014600.

Respectfully submitted,

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